

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>ID0983K</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 01/ 01187</b>	International filing date (day/month/year) <b>12/01/2001</b>	(Earliest) Priority Date (day/month/year) <b>12/01/2000</b>
Applicant <b>SCHERING CORPORATION</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the **title**,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.

because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

1

None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/01187

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-24 all compl. 30, 33,34 all partially

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-24 (all completely); 30,33,34 (all partially)

An isolated nucleic acid comprising an everninomicin biosynthetic pathway gene product from *Micromonospora carbonacea*, e.g., comprising a coding sequence from SEQ ID NO:1 according to the sequences listed in Table 1a and 1b, e.g., wherein the gene product is involved in orsellinic acid biosynthesis or in sugar biosynthesis, or wherein the gene product is a glycosyltransferase, a tailoring enzyme, a regulatory gene product, or wherein the gene product is involved in a resistance mechanism. Vectors and host cells containing said nucleic acids, and methods for expressing said gene products. An isolated polypeptide which is an everninomicin biosynthetic pathway gene product, e.g., according to SEQ ID NOs 2-88 and 96-106. A modified *Micromonospora carbonacea* wherein an everninomicin biosynthetic pathway gene is knocked-out, or wherein an everninomicin biosynthetic pathway gene (e.g., a bottleneck gene) is over-expressed. A vector containing a *Micromonospora carbonacea* everninomicin pathway resistance gene product and a method of selecting for a transfected or transformed host cell using said vector.

2. Claims: 25-29,31,32 (all completely); 30,33, 34 (all partially)

An isolated nucleic acid (e.g., according to SEQ ID NO:90), encoding a *Micromonospora* site-specific integrase (e.g., according to SEQ ID NO:89). A vector for integration comprising said nucleic acid. Said vector, comprising a heterologous gene operatively associated with an expression control sequence. A method for introducing a heterologous gene into an actinomycete (e.g., into *Micromonospora*) using said vector.

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C12N15/52	C12N15/31	C12N15/76	C12N15/90	C12N9/22
	C12N1/21	C12P19/04	C12P19/60		

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C12P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EMBL, EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>DECKER H ET AL.: "A general approach for cloning and characterizing dNDP-glucose dehydratase genes from actinomycetes." FEMS MICROBIOLOGY LETTERS, vol. 141, no. 2-3, 1996, pages 195-201, XP001010562 ISSN: 0378-1097 abstract page 195, left-hand column, line 1 -page 196, left-hand column, line 16 figure 2; table 1 page 200, left-hand column, line 14-27</p> <p>---</p> <p style="text-align: center;">-/-</p>	1-22, 30, 33, 34

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

### ° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

7 August 2001

Date of mailing of the international search report

12.8.01

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo n  
Fax: (+31-70) 340-3016

Authorized officer

van de Kamp, M

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International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BECHTHOLD A ET AL.: "Oligosaccharide antibiotics: perspective for combinatorial biosynthesis" 1999, IN: BIOORGANIC CHEMISTRY, DIEDERICHSEN U. ET AL. (EDS) WILEY-VCH VERLAG GMBH, WEINHEIM, GERMANY XP002173417 page 313-321 ---	1-22,30, 33,34
A	GAISSER S ET AL.: "Cloning of an avilamycin biosynthetic gene cluster from Streptomyces viridochromogenes Tu57." JOURNAL OF BACTERIOLOGY, vol. 179, no. 20, 1997, pages 6271-6278, XP002173414 ISSN: 0021-9193 cited in the application the whole document ---	1-22
A	MALPARTIDA F ET AL.: "Homology between Streptomyces genes coding for synthesis of different polyketides used to clone antibiotic biosynthetic genes" NATURE, vol. 325, 26 February 1987 (1987-02-26), pages 818-821, XP002075972 abstract ---	
A	WO 97 13777 A (SCHERING CORP) 17 April 1997 (1997-04-17) the whole document ---	
A	FOSTER D R ET AL.: "Pharmacologic and bacteriologic properties of SCH-27899 (Ziracin), an investigational antibiotic from the everninomicin family." PHARMACOTHERAPY, vol. 19, no. 10, October 1999 (1999-10), pages 1111-1117, XP001010659 ISSN: 0277-0008 abstract ---	
A	DATABASE WPI Section Ch, Week 199130 Derwent Publications Ltd., London, GB; Class B04, AN 1991-218448 XP002173418 & JP 03 139284 A (TOYO JOZO KK), 13 June 1991 (1991-06-13) abstract ---	23,24
		-/-

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KOCH C ET AL.: "Intrageneric relationships of the actinomycete genus <i>Micromonospora</i> ." INTERNATIONAL JOURNAL OF SYSTEMATIC BACTERIOLOGY, vol. 46, no. 2, 1996, pages 383-387, XP001014515 ISSN: 0020-7713 abstract table 1 ---	1
A	WO 95 16046 A (PERNODET JEAN LUC ;HAGEGE JULIETTE (FR); FRIEDMANN ANNICK (FR); GU) 15 June 1995 (1995-06-15) cited in the application the whole document -----	

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/01187

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
WO 9713777	A 17-04-1997	US AU AU CA EP HU JP JP NZ WO	5780442 A 703452 B2 7383796 A 2234164 A1 0871639 A1 9902644 A2 11507393 T 3199748 B2 320971 A 9713777 A1	14-07-1998 25-03-1999 30-04-1997 17-04-1997 21-10-1998 29-11-1999 29-06-1999 20-08-2001 30-08-1999 17-04-1997
JP 3139284	A 13-06-1991	JP	2912423 B2	28-06-1999
WO 9516046	A 15-06-1995	FR AU AU CA EP WO JP NZ US ZA	2713658 A1 686707 B2 1193595 A 2177600 A1 0788549 A1 9516046 A1 9506257 T 277049 A 5741675 A 9409807 A	16-06-1995 12-02-1998 27-06-1995 15-06-1995 13-08-1997 15-06-1995 24-06-1997 22-09-1997 21-04-1998 01-04-1996